IDEA
International Dialogue for the Evaluation of Allergens

Recommendations of the IDEA Workshop on

Risk Assessment of Pre- & Pro-Haptens

May 28-29, 2013

1) Analytical development:

IFRA AWG[1]: First, the group will select and ensure the general availability of a suitable range of pure references resulting from abiotic transformation of fragrance ingredients; this step implies the development of procedures to prepare and purify haptens currently not commercially available. Furthermore, and because some products of abiotic transformation may be unstable (i.e. hydroperoxides), the IFRA AWG will also assess the half-life of these chemicals as well as any other parameters related to their conservation.

IFRA AWG: These references will be used to develop new analytical methods for the detection and the quantification of chemically-defined haptens, resulting from abiotic transformations, in fragranced products. These methods will have to be sensitive, specific and target limits of quantification below the estimated induction levels and limits of detection below the estimated elicitation levels.

IFRA AWG and RIFM: With the assistance of the workshop participants, the IFRA AWG and RIFM will try to make all relevant haptens resulting from the abiotic transformation of fragrance ingredients readily available for patch-testing. In case of success, these new patch-testing references will be presented to the dermatology community and potentially introduced in patch test baseline series.

2) Risk assessment

RIFM: A suitable SAR tool(s) will be developed to identify likely pre- and pro-haptens. RIFM will contract experts of the chemical reactivity to set and refine structural rules for the identification of materials likely to undergo abiotic transformations. These rules would be incorporated into existing models such as ToxTree.

[1] The IFRA Analytical Working Group (AWG) will supervise all action points related to chemical synthesis and analytical developments. The practical execution of the action items will be ensured by a contract laboratory, or placed under the collective responsibility of the group depending on the type of work involved.

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RIFM: A task force of experts will be convened to characterize and develop human skin models for studying hapten formation, protein interactions and subsequent fate. These models, possibly based on the HR MAS-NMR technique and Skin-Like Cytochrome P450 Cocktail, will be used to assess the risk that pro-haptens represent for the consumer.

RIFM: Based on chemical, cellular, and molecular understanding of dermal sensitization, an exposure-based quantitative risk assessment (QRA) can be conducted to determine safe use levels of fragrance ingredients in different consumer product types. RIFM will review the available pre- and pro- haptens potency and exposure data in view to include concerned fragrance ingredients in the development of the QRA. The recommendations made on pre- and pro-haptens will be taken into consideration when refining the QRA methodology.

IDEA Management Team: The workshop participants recommended that the industry develops strategies for bridging the knowledge gap between induction and elicitation. This recommendation was taken into consideration for the organization of the third IDEA workshop dedicated to the characterization of fragrance allergens (August 28-29, 2013). From now on, the link between induction and elicitation will be studied by this group and all progresses made reported to all idea workshop groups.

3) Risk management

IFRA: Once fully developed and validated, the methods developed by the IFRA AWG will be transferred to a contract laboratory in view to analyze marketed products for haptens presence. This cyclic survey will contribute to determine the actual consumer exposure to haptens. The consumer exposure estimated for each selected hapten will be compared to the clinical prevalence of skin sensitization to this hapten and potentially used to feed the risk assessment process. Furthermore, the results of this survey will play an important role for the post-marketing risk management: companies responsible for products containing problematic concentrations of haptens will be informed and encouraged to correct the situation.

IFRA and other trade associations: A task force will be formed with the help of other trade associations (such as Cosmetics Europe and PCPC) to examine how pre-hapten conversion to haptens can be minimized by improved formulation and storage. This group will consider all aspects of the supply chain (formulation, packaging, storage, etc.) and act quickly to implement optimal practices throughout the industry.